UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/611,902	07/03/2003	Hiroshi Takeyama	Q76104	8672

23373 7590 08/15/2008

SUGHRUE MION, PLLC
2100 PENNSYLVANIA AVENUE, N.W.
SUITE 800
WASHINGTON, DC 20037

EXAMINER	
ANDERSON, JAMES D	

ART UNIT	PAPER NUMBER
1614	

MAIL DATE	DELIVERY MODE
08/15/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/611,902	TAKEYAMA ET AL.	
	Examiner	Art Unit	
	JAMES D. ANDERSON	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 April 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,16 and 17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,16 and 17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Formal Matters

Applicants' response and amendments to the claims, filed 4/14/2008, are acknowledged and entered. Claims 1-3 and 16-17 are pending and under examination.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3 and 16-17 are rejected under 35 U.S.C. § 103(a) as being unpatentable over **"The antitumor effect to stomach cancer by benzyl alcohol,"** Meeting of Japan Surgical Society on April 12-14, 2000, issued on March 10, 2000, PP-1457 (listed on PTO Form 1449, dated October 27, 2003, with a translation provided by Applicant), hereafter referred to as "Reference PP- 1457" and **Head, K.A.** (Alternative Medicine Review, 1998, vol. 3, no. 3, pages 174-186) in view of **Casciari *et al.*** (U.S. Patent No. 6,448,287 B1; Issued 9/10/2002).

The instant claims recite a method of treating a stomach tumor comprising administering benzyl alcohol at a dose of 1 to 50 mg/cm^3 of tumor volume in combination with vitamin C, wherein the ratio of benzyl alcohol to vitamin C is about 1:10.

Reference PP-1457 teaches administration of 200, 300, 400, 500, and 1000 μg benzyl alcohol to cells of the stomach cancer cell line STKM ("Method"). 300 μg or more of benzyl

alcohol resulted in "mortality" of the STKM cells ("Result"). The apoptosis induced by benzyl alcohol in the stomach cancer cell line *in vitro* was induced by 1/3000 of the maximum permissible dose in a human, thus suggesting and motivating higher doses ("Consideration"). The reference further suggests that further *in vivo* testing is required and that benzyl alcohol may be used as an anti-tumor agent, thus motivating *in vivo* treatment of stomach tumors (*id.*). With respect to "external administrating" as recited in instant claim 2, adding the benzyl alcohol to the cultured cells in their dish would include externally administering the composition; in other words, the reference does disclose application of the benzyl alcohol directly onto the cells. The reference also states:

> **"Since we found out that Benzyl alcohol had antitumor effect to a stomach cancer, we report said effect herein"**

which, absent factual evidence to the contrary would suggest *in vivo* treatment and since the gut space is "external" to the body, would have been anticipated as a method of external administration. The reference does not teach or suggest administering benzyl alcohol in combination with vitamin C for the treatment of stomach tumors.

However, Head reviews the use of ascorbic acid (*i.e.*, vitamin C) in the prevention and treatment of cancer. Proposed mechanisms of action for ascorbic acid in the prevention and treatment of cancer include enhancement of the immune system, stimulation of collagen formation necessary for "walling off" tumors, inhibition of hyaluronidase which prevents metastasis, prevention of oncogenic viruses, enhancement of the effect of certain chemotherapeutic drugs, prevention of free radical damage, and neutralization of carcinogenic substances (Abstract). Head reviews several clinical studies on the use of vitamin C in the treatment of cancer patients (pages 176-180), including the instantly claimed stomach cancer (Table 1). In conclusion, Head suggests that while vitamin C alone may not be enough of an intervention in the treatment of most active cancers, since it appears to improve quality of life and extend survival time, it should be considered as a part of a treatment protocol for all patients with cancer (page 184). The reference thus suggests and motivates the addition of vitamin C to existing chemotherapy regimens.

The instantly claimed method of treating stomach tumors with benzyl alcohol and vitamin C would have been *prima facie* obvious at the time the invention was made. Benzyl

alcohol was known to be effective in inducing apoptosis of stomach cancer cells at doses of 200, 300, 400, 500, and 1000 μg. Vitamin C has shown efficacy in the treatment of numerous cancers in human patients, including the instantly claimed stomach cancer and is further suggested as an additive to existing treatment protocols. As such, one skilled in the art would have been imbued with at least a reasonable expectation that the combination of benzyl alcohol and vitamin C would be effective in treating stomach tumors. With respect to the claimed dose of benzyl alcohol (*i.e.*, 1 mg to 50 mg/cm^3 tumor volume) and amount of vitamin C (about 10 parts per 1 part benzyl alcohol), such amounts are not seen as inventive over the prior because they would have been elucidated *via* routine dosing optimization. In this regard, Casciari *et al.* is provided as evidence that vitamin C can be administered in a ratio of 1:1 to 3500:1, preferably 10:1 to 100:1 with another drug (col. 2, lines 15-19).

Applicant's arguments filed 4/14/2008 have been carefully considered but they are not persuasive.

Firstly, Applicants allege that the references alone or in combination do not teach or suggest each limitation recited in claim 1. In support of this allegation, Applicants focus on the teachings of Casciari regarding the amount of Vitamin C in combination with lipoic acid and state that Casciari does not teach or suggest the use of Vitamin C with benzyl alcohol nor the use of Vitamin C and benzyl alcohol in a specific range. However, the Examiner relies on Casciari only with regard to the teaching that Vitamin C, when combined with another drug for treating cancer, is provided in a greater amount (*e.g.*, preferably 10:1 to 100:1) than the other chemotherapeutic drug, thus motivating the use of this ratio in the presently claimed method.

Secondly, Applicants argue that the claims are patentable over the prior art in view of the amendment to claim 1 and in further view of Dr. Takeyama's Declaration under 37 C.F.R. 1.132, filed April 14, 2006. Applicant asserts that the results provided in the Declaration are commensurate in scope with the present claims. However, contrary to Applicant's assertion, the results provided in the Declaration are in fact not commensurate in scope for the following reasons: (i) the experiments in the Takeyama Declaration are *in vitro*, as opposed to the *in vivo* methods instantly claimed; (ii) the doses of benzyl alcohol used in the Takeyama Declaration are 931, 465.5, 232.8, 116.4, 58.2, and 29.1 μg/mL, whereas the doses of benzyl alcohol in the

instant claims range from 1 mg to 50 mg/cm^3 of tumor volume; (iii) the ratio of benzyl alcohol to Vitamin C in the Takeyama Declaration is exactly 1:10, whereas in the instant claims, the ratio is "about 1:10".

The combination of references used in the present rejection teaches, suggests, and motivates the *in vivo* treatment of stomach tumors with the claimed combination of benzyl alcohol and Vitamin C. Accordingly, in the absence of a direct comparison between benzyl alcohol, Vitamin C, and benzyl alcohol + Vitamin C in the treatment of a stomach tumor *in vivo*, using the doses instantly claimed, the Examiner is not persuaded that an unexpected result has been shown that is commensurate in scope with the claims.

Accordingly, the claims are deemed properly rejected because the prior art teaches that benzyl alcohol is effective in the treatment of stomach tumors and further suggests that vitamin C should be used as a part of treatment for all patients with cancer.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JAMES D. ANDERSON whose telephone number is (571)272-9038. The examiner can normally be reached on MON-FRI 9:00 am - 5:00 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/James D Anderson/
Examiner, Art Unit 1614

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614